REMARKS

Claims 1-16 remain under active prosecution in the present application. Applicants respectfully assert that all amendments are supported by the original disclosure and do not introduce new matter. Moreover, Applicants further respectfully assert that the amendments merely clarify the scope of the claims.

In the subject Office Action dated July 7, 2005, please consider the following remarks.

Claim Rejections - 35 USC § 102

The Examiner has now withdrawn the earlier rejection Claims 1- 10 as being anticipated by Reiter et al (US 20047 0023316 Al) in light of the amendment of the claims to recite a new phrase "wherein such antigen specific antibodies bind to the *H. pylori* antigen and do not react with different species and strains of Helicobacter or Campylobacter". Applicants appreciate Examiners cooperation in this matter.

The Examiner has now withdrawn the rejection of claims 11-16 under 35 U.S.C. 102(e) as being anticipated by Reiter et al. (US 20047 0023316 Al) as now traversed. Applicants appreciate Examiners cooperation in this matter.

The Examiner now contends that claims 11-16, do not depend from amended claim 1, and therefore do not recite the combination of claim limitations used to traverse the instantly claimed invention "wherein such antigen specific antibodies bind to the H. pylori antigen and do not react with different species and strains of Helicobacter or Campylobacter". Claims 11-16 have now been amended to make the claims consistent with claim 1.

The Examiner has stated that it is her position that the term "specific" recited in the claims defines a continuum of specificities, and not an absolute binding specificity for a single bacterial pathogen, but defines specific binding to its antigen without non-specific binding. The Examiner stated that all antibodies specifically bind to the antigen to which they were raised, but may also bind to the same antigenic epitope from other sources.

The Examiner now contends that Meyer et al (PG-Pub 2003/01800330) teaches the presence of a number of antigens that will induce antibodies that will immunoreact with more than one strain or species of bacteria (see Meyer et al. paragraph 0086; 0127; 0137; 0139 and 0273).

Applicants respectfully disagree. It appears that the Examiner is imposing her own definition of "specific" as used in the instant specification whenever it is not proper for her to construe the term as such. Applicants believe that the Examiner is misconstruing the term "specific" and has interpreted as a "continuum of specificities and not an absolute binding specificity for a single bacterial pathogen, but defines the specific binding to its antigen without non-specific binding"

While it is correct that antibodies specifically bind to the antigen to which they were raised, and *may* also bind to the same antigenic epitope from other sources, that is not the present invention. The point here is that the antibodies required in the present invention are:

(a) polyclonal/monoclonal *H. pylori* antigen specific antibodies, and

(b) a genus directed monoclonal antibody that reacts with different species and strains of *Helicobacter* or *Campylobacter* and also binds to *H. pylori* antigen. Two different types of antibodies.

The *H. pylori* antigen specific antibodies *only* need to be antigen specific antibodies that

bind to *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter* – it is not required that these antibodies do not react with different species and strains of *any* other bacteria.

The term "specific" is exactly as it is stated and does not includes a continuum of specificity (low, moderate or high specificity), and is limited to the relative lack of reactivity with other strains and species. The claims have now been amended to eliminate the matter phrase "wherein such antigen specific antibodies bind to *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter*" since it is inherent in the specification that *H. pylori* antigen specific antibodies are those specific to *H. pylori* do not react with different species and strains of *Helicobacter* or *Campylobacter*. The previously added phrase was added in order to help the Examiner understand the term but is unnecessary in light of the complete description.

One skilled in the art would understand that, in order for the invention to work, the antigen specific antibodies bind to *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter*. It is obvious in light of the description of the invention that *H. pylori* antigen specific antibodies are specific to *H. pylori*, otherwise, they would have been described as *H. pylori* antigen antibodies. There would have been no need for the term "*specific*." As the Examiner has pointed out, the Examiner stated that all antibodies specifically bind to the antigen to which they were raised. That is why all antibodies are not called antigen specific, only the antibodies that are antigen specific are labeled as such.

As shown in the literature, there are unique epitopes for bacterial pathogens that are *specific* or unique to a species or genus of organisms. The term "specific" has been utilized in

immunological testing methods for years. In fact, there are assays currently available on the market for the detection of various disease states using genus and type specific monoclonal antibodies. These include: specific antibodies for the identification of enteroviruses by immunofluorescence techniques, the screening of adenovirus in stool samples by specific monoclonal antibodies in a antibody based immunoassay, and testing for Chlamydia by genus specific and species specific IgGs have been described. Applicants have enclosed literature references for the Examiners consideration.

In addition, United States Patent No. 4,950,589 by Butman, *et al.*, shows a patented genus-specific lysteria antigen as identified by genus specific monoclonal antibodies. *Helicobacter pylori* is fairly unique in the fact that when it originally was discovered it was placed genus *Campylobacter* because of various characteristic traits that it shared with *Campylobacters*. Later it was discovered that it was its own unique organism and it was moved into its own genus *Helicobacter*.

In the present application, the antigen-specificity of any particular antibody can be readily assessed using routine laboratory methods. In general, specificity of an antibody is confirmed by ELISA testing of the antibodies against a comprehensive panel of relevant organisms. Those antibodies that fail to react significantly with any of the non-specific organisms tested can be concluded that they are specific.

In regards to the Meyer patent (PG-P2003/01800330), the Examiner refers to specific paragraphs—namely 0086, 0127, 0137, 0139 and 0273 in her discussion. There is a fundamental difference between the way bacterial strains are used for the inducement of an antibody response versus using an antibody strain to detect circulating antibody in people who

have been infected with *Helicobacter pylori* (as described in the Meyer patent). It has been known for years that when one tests serum from various patients that are positive for *Helicobacter pylori*, the method by which they extract antigens from *Helicobacter* strains will influence the data generated with that immune serum. However, there is a totally different response if one controls the injection or the immunization process of an animal versus a naturally occurring infection in a human. The reference in Meyer, in fact, specifically isolates *Helicobacter* proteins utilizing the cell extracts comprising solubilized materials. Much of the work they do, especially in claims 22 and 23 talk about using cell extracts and using denaturing agents to assist in the expression of these solubilized proteins. This is quite different than the method described in our patent.

The teachings of Meyer do not teach that a diagnostic application can be made utilizing specific capture systems specific to the genuses *Helicobacter* and/or *Campylobacter*. What Meyer teaches is that there are additional proteins found in *Helicobacter* that may also be found in other bacteria, such as, *H. influenza*, *P. aeurginosa* and *C. jejuni* for instance. What Meyer teaches is that these proteins should be avoided for use in developing vaccines or other diagnostic assays to detect serum based antibodies to *Helicobacter*. Our patent outlined a method that directly detects antigens found in various human samples—not antibodies found in human serum. The method for screening primarily found in Meyer uses serum, human serum from patients or people who have been naturally exposed to *H. pylori*. This is not the teaching as found in our patent.

An important paper to consider in this discussion is a paper that was published by Perez-Perez and Blaser entitled "Conservation and Diversity of *Campylobacter pyloridis* Major

Antigens", *Infection and Immunity*, May 1987, p. 1256-1263. This paper demonstrates both aspects as we are trying to prove, or show, in our patent. There is both conservation of antigens and diversity of antigens that are found within the genus and species *Helicobacter (Campylobacter) pylori*. Their observations were, "Whole-cell and outer-membrane proteins observed in all strains of *Campylobacter pyloridis* (*Helicobacter pylori*) were nearly identical; none were similar to those of *C. jejuni* and *C. fetus.*" However, when they acid extracted proteins from *H. pylori* these antigens they showed similarities between the acid extracted proteins of *C. jejuni*. Because various antigens that are found on *Helicobacter pylori* are conserved, polyclonal antibodies can be raised that exhibit unique specificity for the *Helicobacter pylori* bacterium. In addition, because there is some genetic diversity, there are other antigens that potentially are conserved within the genuses *Campylobacter* and *Helicobacter*. This is borne out in this paper since there are specific reactions unique to both *Campylobacter jejuni* and *Helicobacter pylori* while other responses are highly specific to *Helicobacter pylori* only. Highly specific polyclonal antibodies have been known for many years and is demonstrated by many other products that are commercially viable. For example: Polyclonal antisera is used for Salmonella O typing; anti-sera to Groups A, B, C, E, F and G are used to distinguish these organisms from each other when in fact they are from the same genus and species. The same is true for Salmonella H typing as well. Polyclonal antisera is still being used to differentiate streptococcus Group A, B, C, D and F from each other without unwanted cross-reactions. What the authors are trying to claim in this paper is that there are unique conserved antigens within genus *Helicobacter* and/or *Campylobacter*. One can exploit this to develop a broad based detection system or capture system in a ELISA based technology and use

a second level of antibodies to generate the specificity as it relates specifically to the genus species *Helicobacter pylori.*

The example of an antibody that would fall under the definitions as implied by this patent can be found in a paper written by D.G. Newell entitled "Monoclonal antibodies directed against the flagella of *Campylobacter jejuni*: cross-reacting and serotypic specificity potential use in diagnosis". Within this paper Newell describes an antibody that he calls cross-reacting antibody CF5. This monoclonal antibody not only reacted with most of the species within the genus *Campylobacter*, it also reacted with, as he described, the gastric *Campylobacter*-like organism – *Campylobacter pyloridis*. In addition, he demonstrated that the antibody was specific for the genus *Campylobacter* (or in the case of *pylori Helicobacter*) because when tested against *E. coli*, Proteus, Pseudomonas, *S. typhimurium* and *V. cholerae* they did not observe any unwanted reactions. This is a monoclonal antibody that would be useful and defined by our patent. The CF5 antibody could be used as a capture system, which would have the ability to capture not only *Helicobacter pylori* but other *Campylobacters* as well. The specific polyclonal antibody directed against only *Helicobacter pylori* would then be employed to give the assay its unique specificity to *Helicobacter.*

Thus, is respectfully submitted that the present specification fully meets the requirements of 35 U.S.C. 102 and withdrawal of these rejections is respectfully requested.

Claim Rejections - 35 USC § 112

The Examiner has rejected claims 1-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, claims 1-10 have been amended to recite the phrase ""wherein such antigen specific antibodies bind to the *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter*." The Examiner contends that this phrase does not evidence original descriptive support in the instant specification. The Examiner now contends that all of the claims recite a combination of claim limitations for which the instant Specification does not provide original descriptive support and therefore recite New Matter.

Applicants respectfully disagree. The current Specification provides for adequate support as described above. That is, the term "specific", when used in context of the present Specification in the phrase *H. pylori* antigen antibodies inherently means specific to *H. pylori.* As described above, one skilled in the art would understand that, in order for the invention to work, the antigen specific antibodies bind to *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter*.

Paragraphs 0012 and 0013 show that the invention uses employs genus specific monoclonal antibodies which "can cross-react with different species and strains of *Helicobacter* or *Campylobacter*." Inherently, the H. pylori antigen specific antibodies are not genus-specific and *do not* cross-react with different species and strains of *Helicobacter* or *Campylobacter*. Hence, the different naming of the antibodies.

Applicants contend that the phrase "wherein such antigen specific antibodies bind to *H. pylori* antigen and do not react with different species and strains of *Helicobacter* or *Campylobacter*" is inherent in the application, is unnecessary to understand and practice the

present invention, and was only added for clarification for the Examiner's sake. The Examiner is invited to delete this phrase from all claims through an Examiner's amendment, if she feels it would avoid any ambiguity.

Thus, is respectfully submitted that the present specification fully meets the requirements of 35 U.S.C. 112 and withdrawal of these rejections is respectfully requested.

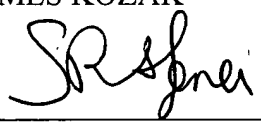
CONCLUSION

In light of the amendments and remarks made herein, it is respectfully submitted that the claims currently pending in the present application are in form for allowance. Accordingly, reconsideration of those claims, as amended herein, is earnestly solicited. Applicants encourage the Examiner to contact their representative, Stephen R. Albainy-Jenei at (513) 651-6839 or salbainyjenei@fbtlaw.com.

The Commissioner for Patents is hereby authorized to charge any deficiency or credit any overpayment of fees to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

KENNETH JAMES KOZAK

By 

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